Relief of severe left ventricular outflow obstruction in a case of hypertrophic obstructive cardiomyopathy treated with practolol

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The clinical and haemodynamic findings in a patient with hypertrophic obstructive cardiomyopathy and severe left ventricular outflow obstruction are presented. Treatment with an increasing dose of orally administered practolol up to a maximum of 1200 mg a day, resulted in symptomatic improvement, and abolition of the resting gradient when the patient was recatheterized six months later.

Case report

A 46-year-old white woman was first seen on 28 December 1972. For the previous 6 months she had experienced attacks of tightening left pectoral pain on exertion, which slowly progressed in severity.

A month before examination she noted breathlessness on exertion and while cycling she suffered from an attack of acute shortness of breath, during which she sweated profusely and was noted to be very pale. On further questioning, she did not suffer from palpitations, dizziness, or fainting attacks. She had no past history of rheumatic fever.

Family history

She has 2 brothers and 4 sisters in Switzerland, who are in good health as far as she knows. Her father died at the age of 75; the cause of death is not known. On examination, the jugular venous pressure was normal, pulse regular, femoral artery pulsations palpable without delay, blood pressure 150/90 mmHg. On examination of the heart, a double left ventricular impulse was noted in the fifth intercostal space in the midclavicular line. On auscultation there was a loud fourth sound at the apex and over the lower sternal edge, and a grade 3/6 ejection type murmur, loudest between the apex and the lower sternal edge; at the base the murmur was soft (grade 1 to 2/6), not radiating to the carotid arteries. The second sound was closely split. Further physical examination was uninformative. Chest x-ray showed a heart of normal size and configuration (cardiothoracic ratio 13/28.5). The hila and lung fields were normal.

Electrocardiogram (Fig. 1A) showed sinus rhythm, PR interval 0.12 sec, notched P waves, left ventricular hypertrophy and strain pattern. Phonocardiogram showed prominent fourth sound in the frequency range 35 and 70 Hz. There was an ejection systolic murmur of maximal intensity between the lower sternal

edge and the apex; it ended before a closely split second sound. Carotid pulse recording showed a rapid upstroke time 0.05 sec followed by a second rounded wave in late systole. Systolic ejection time 0.30 sec. Jugular venous pulsations showed prominent a waves. Apex-cardiogram showed large A waves, 20 per cent of the total deflection.

Cardiac catheterization was done on 4 January 1973 (Table, Fig. 2). Right and left heart studies were performed. Left ventricular pressure was measured in the inflow via transseptal catheter; ascending aortic pressure was recorded via a catheter introduced into the right femoral artery by the Seldinger technique. Pertinent haemodynamic data included: left atrial mean pressure 17 mmHg, left ventricular systolic pressure 250-280 mmHg, end-diastolic pressure 23-30 mmHg, maximal dp/dt 4600 mmHg per sec, ascending aorta pressure 148/68 mmHg, peak systolic pressure gradient at rest 132 mmHg, heart rate 114 a minute, cardiac index 3.06 litres/min per m², stroke index 25.5 ml/m². Ten minutes after injection of 20 mg practolol intravenously, the left ventricular systolic pressure fell to 208 mmHg, aortic systolic pressure was 136 mmHg, peak systolic gradient 72 mmHg, left ventricular end-diastolic pressure 18 mmHg, heart rate 94 a minute. Left ventricular cineangiogram in the left lateral position showed a small left ventricular cavity with a thickened wall. There was severe obstruction of the outflow of the left ventricle by a hypertrophied locally protruding septum, resulting in a well-defined subaortic chamber. There was grade 3 mitral regurgitation, but there were a number of ventricular extrasystoles during contrast injection in the left ventricle.

Treatment was begun with practolol twice daily, 100 mg, and increased to twice daily, 200 mg, on discharge (9 January 1973). The case was subsequently discussed at the Cardiothoracic Unit of the Antonius hospital in Utrecht, when it was decided to continue

FIG. 1 Electrocardiograms (A, 1 January 1973; and B, 6 June 1973) showed considerable improvement in the left ventricular abnormality on 6 June 1973.

FIG. 2 Simultaneous recording of left ventricular inflow and ascending aorta pressure. A) 4 January 1973; B) 7 June 1973. Loss of left ventricular outflow tract gradient when the patient was reinvestigated on 7 June 1973 is shown.

temporarily with beta-blockers in view of the significant reduction in the systolic gradient after intravenous injection.

The dose of practolol was increased at monthly intervals by 200 mg, up to a maximum daily dosage of 1200 mg, which she continues to take up to the present time. During the first three months she was advised to take things easily. After three months restrictions on her

physical activity were eased because she was feeling well, and on clinical examination there were signs of improvement.

In June 1973 she was admitted to hospital in order to reassess her cardiac status. On examination her venous pressure was normal, pulse 72 a minute regular, blood pressure 140/90 mmHg. There was no cardiac enlargement; on auscultation there was a grade 2/6 midsystolic

TABLE Haemodynamic data

	RV	LA mean	LV S/d/max dp/dt	Ao S/D	LV-Ao	HR/min	Cardiac index (l./min per m ²)	Stroke index (ml/stroke per m ²)
4 January 1973								
Rest	46	17	280,23,4600 mmHg/sec	148/68	132	114	3.06	25.5
10 minutes after practo- lol 20 mg i.v.	—	—	208,18	136/72	72	94	—	—
7 June 1973								
Rest	24	2.5	122,11,2200 mmHg/sec	122/70	0	76	3.44	45
Exercise 5 minutes	—	—	160-176, 15	140-152	12-24	110	3.1	28
Isoprenaline 20 µg i.v.	—	—	164, 12-14	126/68	38	76	—	—

Abbreviations: RV=right ventricular pressure (mmHg); LA mean=left atrial mean pressure (mmHg); LV=left ventricular pressure (mmHg), S=systolic, D=diastolic, ed=end-diastolic; LV-Ao=left ventricular-aortic pressure gradient (mmHg); HR=heart rate per minute.

ejection murmur maximal between the apex and the lower sternal edge. A fourth heart sound was no longer audible.

Electrocardiogram (Fig. 1 B) indicated sinus rhythm, PR 0.20 sec, inverted T waves in lead aVL, but no further abnormalities. All signs of left ventricular hypertrophy and strain had regressed. Compared to the record of January 1973, the phonocardiogram showed that the midsystolic murmur was shorter in duration and lower in amplitude (identical gain on the pick-up microphone was used during both recordings). The fourth sound was much smaller. The upstroke time of the carotid curve was now longer, 0.08 sec, and ejection time was 0.30 sec. There was a change in the shape of the carotid pulse tracings; in only occasional recordings was there a small secondary rounded wave in late systole. On the apex cardiogram the A waves were now 13 per cent of the total deflection. On chest x-ray the heart remained unchanged in size and shape (cardiothoracic ratio 13/28.5). The hila and lung fields were normal. Repeat cardiac catheterization on the 7 June 1973 (Table) revealed a right ventricular systolic pressure of 24 mmHg, left atrial mean pressure of 2.5 mmHg, left ventricular systolic pressure 122 mmHg, end-diastolic pressure 11 mmHg, maximal dp/dt 2200 mmHg per sec, and ascending aortic pressure 122/70 mmHg. On simultaneous recording of the left ventricular and ascending aortic pressure at rest, there was no systolic gradient. Pulse rate at rest was 76 a minute, cardiac index 3.44 l./min per m², and stroke index 45 ml/m². During exercise (straight leg raising for 5 minutes) the heart rate increased to 110 a minute, cardiac index was 3.1 l./min per m², and the stroke index was 28 ml/m². Simultaneous recording of left ventricular and ascending aortic pressure after 5 minutes of straight leg raising revealed a systolic gradient that varied between 12 and 24 mmHg; the heart rate was 94 a minute. In post-extrasystolic beats the gradient was 60 mmHg. Left

ventricular end-diastolic pressure during exercise was 15 mmHg. A total dose of 20 µg isoprenaline was intravenously injected without any acceleration of the heart rate; however, a systolic gradient of 38 mmHg developed. Left ventricular cineangiography was repeated in the left lateral position, and there was no change in the appearance of the left ventricle and outflow tract when compared with the angiogram of January 1973.

The patient was discharged, and treatment was continued with 1200 mg practolol daily. She was last seen at the outpatients' department on 4 December 1973, when she reported that she was feeling well, with no shortness of breath, and no effort angina. The patient sometimes experiences a mild sensation of pressure in the left pectoral region, but always unrelated to exertion. The only side effects from practolol therapy have been constipation and nightmares, but the latter have not been troublesome lately. The patient continues to take practolol in the same dosage (1200 mg a day) and is being followed up at 3-monthly intervals.

Discussion

The published work on practolol up to date in patients with hypertrophic obstructive cardiomyopathy has shown no significant effect on outflow tract obstruction at rest or with stress (Webb-Peploe, Croxson, and Oakley 1971a; Matlof and Harrison, 1973) but left ventricular end-diastolic pressure was lowered (Webb-Peploe *et al.*, 1971a, b). It is generally accepted that few seriously symptomatic patients with severe outflow tract obstruction can be spared operative treatment by beta-adrenergic blockade.

Contrary to the experience of other workers, practolol 20 mg injected intravenously at the first

catheterization (4 January 1973) significantly diminished the gradient across the outflow tract of the left ventricle (132 mmHg before, and 72 mmHg 10 minutes after). Encouraged by the result, we continued therapy with orally administered practolol in increasing doses up to a maximum of 1200 mg daily. Six months later there were subjective and objective signs of improvement, and when recatheterized the resting gradient across the outflow tract of the left ventricle was abolished.

Further trial of long-term practolol therapy in cases of hypertrophic obstructive cardiomyopathy and severe outflow tract obstruction seems justified.

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